REMARKS

Claims 1, 2, 5-16, 18-25, 50 and 51 were pending in the subject application. Applicant herein above has amended claims 1, 15 and 50. Accordingly, claims 1, 2, 5-16, 18-25, 50 and 51 are presented for the Examiner's consideration.

Support for the amendment to claims 1 and 50 is discussed below in applicant's reply to the rejection under 35 U.S.C. § 112, second paragraph.

Objection to Specification

On page 2 of the August 28, 2003 Office Action, the Examiner objected to the presence of hyperlinks in the specification.

In response, applicant has amended the specification to not contain anything resembling a link, but to instead provide the proper citation to documents obtained in the Internet. Accordingly, applicant respectfully requests that the Examiner reconsider and withdraw this objection.

Rejection under 35 U.S.C. § 112, first paragraph
Enablement

On pages 2-4 of the August 28, 2003 Office Action, the Examiner rejected claims 15-25 under 35 U.S.C. § 112, first paragraph, alleging that the specification, while being enabling for method of expressing foreign DNA in a host cell *in vitro*, does not reasonably provide enablement for methods of expressing foreign DNA in a host cell *in vivo*. The Examiner alleged that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The Examiner noted that the aspects of the previous enablement rejection directed to methods of transforming a host

cell *in vivo* are maintained for the reasons of record advanced on pages 4-6 of the Office action mailed on January 16, 2003; however, the aspects of the previous enablement rejection directed to variants of the promoter sequence of the invention have been withdrawn.

The Examiner stated that applicant's arguments filed April 21, 2003 have been fully considered but they are not persuasive. The Examiner noted applicant's contentions that introduction and expression of recombinant expression constructs in living cells has been known to those skilled in the art for twenty years; that many techniques have been developed for introducing foreign DNA into mammalian cells; and that the claims are enabled to the extent of reading on transformation of living cells. The Examiner, however, maintained that methods of transforming cells *in vivo* are encompassed within the field of gene therapy, and that the art of gene therapy was unpredictable at the time the claimed invention was filed and has remained unpredictable thereafter.

In response, without conceding the correctness of the Examiner's position but solely to advance the prosecution of the subject application, the applicant has amended claims 15-25 to recite cells in cell culture, thereby making the Examiner's concerns moot. Accordingly, applicant's amended claims meet the enablement requirement of 35 U.S.C. 112, and this rejection should be withdrawn.

For the record, however, applicant point out that the preparation of recombinant expression constructs, inserting them into living cells, and expressing the constructs in living cells has been known to those skilled in the art for at least twenty (20) years prior to the filing of the subject application. For example, in

1977, Wigler, M., et al., Cell 11: 223-232 (1977) described transformation of eucaryotic cells, specifically mammalian cells, with foreign DNA coding for a selectable phenotype. Over the years, a number of techniques have been developed for introducing DNA into mammalian cells, e.g. calcium phosphate co-precipitation, DEAE-dextron, microinjection, protoplast fusion, electroporation, lipofection, etc. Therefore, to the extent applicant's claims read on transformation of living cell, the claims are enabled. Furthermore, after making transformed mammalian cells, it is hardly difficult to insert such transformed cell back into the mammal. Indeed, numerous cancer researchers use xenographting to study development of tumors. Thus, applicant finds the Examiner's rejection unfounded in view of this large body of prior art showing *in vivo* transformation of cells.

Rejection under 35 U.S.C. § 112, second paragraph

On pages 5-6 of the August 28, 2003 Office Action, the Examiner rejected claims 1-2, 5-16, 18-25 and 50-51 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner alleged that claim 1 is indefinite as written because the nucleotide sequence set forth in SEQ ID NO:1 does not comprise nucleotides that have negative numbering. As such, the Examiner noted that it is not clear which nucleotide bases of SEQ ID NO:1 correlate to the sequence beginning at bp -469 and ending at bp +101 or to the sequence beginning at bp -101 and ending at bp -32. The Examiner did note that Figure 3, as described on page 7, provides the nucleotide sequence set forth in SEQ ID NO:1 in the context of an actual promoter sequence by depicting the regions of SEQ ID NO:1 that are upstream and downstream of the transcription initiation site. For example the 5' end of the sequence is

position -928 and the 3' end of the sequence is +101; and a Sac 1 restriction site is positioned at -469. However, the Examiner noted that comparison of the sequences of Figure 3 and SEQ ID NO:1 suggests that a discrepancy exists with respect to position -469 (the Sac1 site), specifically in that the Sac1 site as shown in Figure 3 is not at position -469 but rather is at position -471, and also, in that the length of the 5' end of exon 1 as shown by the bolded sequence in figure 3 is longer than 101 bases suggesting that the sequence does not end at position +101 as discussed in the specification on pages 7-8. In light of the above, the Examiner suggested amending the claims to recite a correlation between the exact sequences in Figure 3 and SEQ ID NO:1 as embraced by the claim in steps b and c.

In response, applicant has amended claim 1 and claim 50 to more clearly recite applicant's invention. Applicant thanks the Examiner for pointing out the ambiguity in the claims. Applicant has amended claim 1 and 50 to use the numbering of SEQ ID NO. 1.

Initially, applicants notes that the sequence of SEQ ID NO. 1 corresponds to the sequence set forth in Figure 3 of the subject application. To assist in correlating the nucleotide numbering used in SEQ ID NO.1, which are now also used in amended claim 1, to the markings in the sequence of Figure 3, applicant has reproduced in **Exhibit A** hereto the sequence of SEQ ID NO. 1 and has marked thereon the location of the Sac1 site, the SP1 site and the TATAA box element from Figure 3.

The Examiner will note that directly to the right of the Sac1 site is nucleotide number 624 of SEQ ID NO. 1. Thus, the recitation in amended claim 1 of a nucleotide sequence beginning at bp 624 and ending at bp 1197 of SEQ ID NO: 1 is clear.

The Examiner will also note that the segment of nucleotides in between the SP1 site and the TATAA box element begins with nucleotide number 1005 and ends with nucleotide number 1059 in SEQ ID NO. 1. Thus, the recitation in amended claim 1 of a nucleotide sequence beginning at bp 1005 and ending at bp 1059 of SEQ ID NO: 1 is clear.

To summarize, part a) of amended claim 1 recites the entire sequence set forth in SEQ ID NO. 1 and in Figure 3; part b) of amended claim 1 recites the 5' segment of SEQ ID NO. 1 that is downstream of the Sac1 site shown in Figure 3; and part c) of amended claim 1 recites the segment in between the Sp1 site and the TATAA box element shown in Figure 3. Furthermore, claim 1, as amended, is clearly supported by the subject application.

Accordingly, applicant's amended claims meet the definiteness requirement of 35 U.S.C. 112, and this rejection should be withdrawn.

In view of the above mentioned amendments and remarks, the Applicant requests that the Examiner reconsider and withdraw the rejections set forth in the August 28, 2003 Office Action.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicant's undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the enclosed $55.00 fee for a one-month extension of time, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Gary J. Gershik 12/19/03
John P. White Date
Reg. No. 28,678
Gary J. Gershik
Reg. No. 39,992

SEQ ID NO. 1

acctgagttt tggccagaat aaggtgacat ttagtttgtt ggcttgatgg atgacttaaa 60

tatttagaca tatggtgtgt aggcctgcat tcctactctt gccttttttt ttgcccctcc 120

agtgttttgg gtagttttgc tcccctacag ccaaaggcaa acagataagt tggaggtctg 180

gagtggctac ataattttac acgactgcaa ttctctggct gcacttcaca aatgtataca 240

aactaaatac aagtcctgtg tttttatcac agggaggctg atcaatataa tgaaattaaa 300

aggggctgg tccatattgt tctgtgtttt tgtttgtttg tttctttttt tgtttttgtg 360

gcctccttcc tctcaattta tgaagagaag cagtaagatg ttcctctcgg gtcctctgag 420

ggacctgggg agctcaggct gggaatctcc aaggcagtag gtcgcctatc aaaaatcaaa 480

gtccaggttt gtgggggggaa aacaaaagca gcccattacc cagaggactg tccgccttcc 540

cctcacccca gcctaggcct ttgaaaggaa acaaaagaca agacaaaatg attggcgtcc 600

tgagggagat tcagcctaga gctctctctc cccaatccct ccctccggct gaggaaacta 660

^ SacI

acaaaggaaa aaaaaattgc ggaaagcagg atttagagga agcaaattcc actggtgccc 720

ttggctgccg ggaacgtgga ctagagagtc tgcggcgcag ccccgagccc agcgcttccc 780

gcgcgtctta ggccggcggg cccgggcggg ggaaggggac gcagaccgcg gaccctaaga 840

cacctgctgt accctccacc cccaccccac ccacctcccc ccaactccct agatgtgtcg 900

tgggcggctg aacgtcgccc gtttaagggg cgggccccgg ctccacgtgc tttctgctga 960

gtgactgaac tacataaaca gaggccggga acggggcggg gaggagggag agcacaggct 1020

SP1

ttgaccgata gtaacctctg cgctcggtgc agccgaatct ataaaaggaa ctagtcccgg 1080

caaaaacccc gtaattgcga gcgagagtga gtggggccgg gacccgcaga gccgagccga 1140

cccttctctc ccgggctgcg gcagggcagg gcggggagct ccgcgcacca acagagc 1197